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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte ALICIA SANTOS SAVIO, RICARDO SILVA RODRIGUEZ, YANELIS MORERA DIAZ, ARMANDO ALEXEI RODRIGUEZ ALFONSO, JOSE RAFAEL CASTILLO, HAYDEE GERONIMO PEREZ, ALEJANDRO MORO SORIA, and SILVIO ERNESTO PEREA RODRIGUEZ

Appeal 2010-002392
Application 10/529,923
Technology Center 1600

Before ERIC GRIMES, FRANCISCO C. PRATS, and JEFFREY N. FREDMAN, *Administrative Patent Judges*.

FREDMAN, *Administrative Patent Judge*.

DECISION ON APPEAL[1]

This is an appeal under 35 U.S.C. § 134 involving claims to methods of generating a neutralizing antibody response to IL-15. The Examiner

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[1] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, or for filing a request for rehearing, as recited in 37 C.F.R. § 41.52, begins to run from the "MAIL DATE" (paper delivery mode) or the "NOTIFICATION DATE" (electronic delivery mode) shown on the PTOL-90A cover letter attached to this decision.

rejected the claims as obvious. We have jurisdiction under 35 U.S.C. § 6(b).

We reverse.

Statement of the Case

The Claims

Claims 22 and 23 are on appeal. Claims 22 and 23 read as follows:

> 22. A method for generating a neutralizing antibody response against autologous IL-15 in a primate, wherein said method comprises administering to said primate a composition comprising human IL-15 and aluminum hydroxide, wherein the IL-15 is an antigen and wherein said IL-15 antigen generates neutralizing self-antibodies against IL-15.
>
> 23. The method according to claim 22, wherein the IL-15 antigen is coupled to a carrier protein, and wherein the carrier protein is P64k protein.

The prior art

The Examiner relies on the following prior art references to show unpatentability:

Grabstein et al. WO 95/27722 Oct. 19, 1995

Brewer et al., *Aluminium Hydroxide Adjuvant Initiates Strong Antigen-Specific Th2 Responses in the Absence of IL-4- or IL-13-Mediated Signaling*, 163 J. IMMUNOLOGY 6448-6454 (1999).

González et al., *P64k Meningococcal Protein as Immunological Carrier for Weak Immunogens*, 52 SCANDINAVIAN J. IMMUNOLOGY 113-116 (2000).

The issue

The Examiner rejected claims 22 and 23 under 35 U.S.C. § 103(a) as obvious over Grabstein, González, and Brewer (Ans. 3-6).

The Examiner finds it would have been obvious to the skilled artisan, based on the teachings of Grabstein, Brewer, and González, "to administer a composition comprising human IL-15 and aluminium hydroxide to a primate, wherein the IL-15 may or may not be coupled to P64k protein, for the purpose of generating antibodies specific for IL-15" (Ans. 5).

Appellants contend that they "are claiming a method in which the administration of human IL-15 generates neutralizing self-antibodies against IL-15. None of the cited references disclose or suggest this claimed method" (App. Br. 6-7). Appellants contend that:

> Instead of stimulating T lymphocyte proliferation as disclosed in Grabstein, the claimed neutralizing response would inhibit the activity of IL-15 as a cytokine, as disclosed by Grabstein. The claimed neutralizing response is further demonstrated in the specification in Example 3, in which inhibition of IL-15 induced CTLL-2 proliferation was observed. Grabstein, on the other hand, demonstrates stimulation of CTLL-2 proliferation using IL-15.

(*Id.* at 7-8.)

Appellants also contend that "prior to the application, it was not known that administrating a composition of comprising human IL-15 and aluminum hydroxide could be administered to generate a neutralizing self-antibody against IL-15." (Reply Br. 3.)

The issue with respect to this rejection is: Does the evidence of record support the Examiner's conclusion that Grabstein, Brewer, and González render obvious the generation of neutralizing self-antibodies against IL-15?

Findings of Fact

1. Grabstein teaches a

> novel T-cell growth factor, hereinafter referred to as "Interleukin-15" ("IL-15"), has been isolated and purified. A cDNA sequence encoding a simian IL-15 polypeptide was isolated. . . . The nucleotide sequences and deduced amino acid sequences of simian and human open reading frames are disclosed in SEQ ID NOS 1 and 4.

(Grabstein 2, ll. 29-39.)

2. Grabstein teaches that the "mature IL-15 polypeptide is capable of signaling proliferation and/or differentiation of precursor or mature T-cells. The protein, therefore, can be used to promote long-term *in vitro* culture of T-lymphocytes and T-cell lines" (Grabstein 4, ll. 16-18).

3. Grabstein teaches that for

> therapeutic use, purified IL-15 or a biologically active derivative thereof is administered to a patient, preferably a human, for treatment in a manner appropriate to the indication.

(Grabstein 15, ll. 26-30.)

4. Grabstein teaches that "[t]ypically, an IL-15 therapeutic agent will be administered in the form of a pharmaceutical composition comprising purified polypeptide in conjunction with physiologically acceptable carriers, excipients or diluents" (Grabstein 15, ll. 32-34).

5. Grabstein teaches that "[e]xperiments with PHA [phytohemagglutinin] activated PBT [peripheral blood T-cells] demonstrate that rIL-15 exerts its growth stimulatory effects independently of IL-2, in

that antibodies to IL-2 or to the IL-2 receptor do not inhibit IL-15" (Grabstein, 4, ll. 29-31).

6. The Examiner finds that Grabstein "does not teach administration of a composition comprising human IL-15 and aluminum hydroxide for the purpose of generating a neutralizing antibody response against autologous IL-15" (Ans. 4).

7. Brewer teaches that the "use of aluminium compounds (alum) as vaccine adjuvants is associated with the induction of Th2 responses" (Brewer 6448, col. 1).

8. González teaches that "[o]ur results suggest that recombinant P64k protein could be a readily available immunological carrier, as efficient as other commonly used large carrier molecules" (González 113, abstract).

9. González teaches that "P64k can exert its carrier function absorbed on aluminium hydroxide, one of the few adjuvants widely used in human vaccines" (González 115, col. 2).

Principles of Law

The Examiner has the initial burden of establishing a prima facie case obviousness under 35 U.S.C. § 103. *In re Oetiker*, 977 F.2d 1443, 1445 (Fed. Cir. 1992).

"[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007).

Analysis

We agree with the Examiner that IL-15 is a known polypeptide that may have therapeutic uses (FF 1-5). We can also agree that, generically, when antibodies are desired, the use of alum compounds as adjuvants and the use of fusion proteins as carriers, may well be obvious (FF 7-9).

However, we cannot agree with the Examiner's conclusion that "a person of ordinary skill in the art would have been motivated to administer a composition comprising IL-15 to a primate for the purpose of generating antibodies which would be useful in the isolation and/or characterization of the biological properties of IL-15" (Ans. 5).

This conclusory statement is not supported by the prior art, which entirely lacks any teachings to generate neutralizing antibodies in primates to IL-15. Even the one statement identified by the Examiner in Grabstein, where IL-2 antibodies were shown to not inhibit IL-15 (FF 5) does not state that the antibodies were generated in primates, but more reasonably is interpreted to refer to mouse or rabbit antibodies.

The Examiner has presented no evidence or reason, other than a general desire for further experimentation, to generate neutralizing antibodies to IL-15 in primates. We conclude that a more particularized reason is required in this situation.

We also agree with Appellants that the only therapeutic teachings in Grabstein for IL-15 were to "stimulate the activity of CTL, LAK and NK cells and expand the population of T cells that can destroy tumor cells and viral-infected cells" (Grabstein 24, ll. 14-16). As Appellants note, this teaching does not provide the ordinary artisan with a reason to neutralize IL-

15, but instead suggests treatment based on activating IL-15 (*see* App. Br. 7).

Conclusion of Law

The evidence of record does not support the Examiner's conclusion that Grabstein, Brewer, and González render obvious the generation of neutralizing self-antibodies against IL-15.

SUMMARY

In summary, we reverse the rejection of claims 22 and 23 under 35 U.S.C. § 103(a) as obvious over Grabstein, González, and Brewer.

REVERSED

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